Development of *in-vitro* screening approaches to optimise siRNA formulation performance

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Introduction

Short interfering ribonucleic acids (siRNAs) have attracted significant interest as promising candidates for an entirely new class of next-generation medicines[1]. However, after more than a decade, only a handful of siRNA formulations have reached the stage of clinical trials, mainly due to a dearth of understanding in how siRNA formulation affects efficacy and safety. These difficulties are further exacerbated by the time-consuming and expensive methodologies required for evaluation and optimisation of formulation performance. Such challenges therefore have led to the exploration of high throughput screening (HTS) approaches, to enable rapid selection of the most promising candidate siRNA formulations to take forward into *in-vivo* studies. Recent research within the School has revealed that the pore-forming abilities of nucleic acid-polymer formulations on supported lipid bilayers (SLBs) can be correlated with their transfection efficiency[2]. Within this project we aim to extend this observation to a microarray format, and investigate the potential of SLB microarrays for the HTS of siRNA formulations.

Conclusion and Future Work

The parameters for fabrication of model SLB on mica using two manufacturing techniques have been optimised and characterised. Future work will be focused on optimising the fabrication methodologies and characterisation of model SLBs on microscope slide-sized surfaces. This will include optimisation of the printing techniques required for the production of SLB microarrays and assessments of surfaces to provide air-stable SLBs (e.g. commercially available FluidArray®[3] surfaces). Strategies for the rapid readout of arrays, e.g. based on fluorescence will also be investigated. Eventually, the usefulness of the SLB model will be assessed through comparison of the siRNA formulation interactions with cellular membranes.

References

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